autologous patients that failed prior collection attempts with filgrastim (G-CSF) alone. Many centers use plerixafor for prior failed mobilization on the evening of day 4 of G-CSF. Less consensus regarding the utilization and timing of plerixafor with current ineffective mobilization exists. We developed a strategy utilizing double-dose G-CSF on day 4 if the CD34 count was less than 10 cells/μL in an attempt to increase the CD34 count to sufficient levels to initiate HPC-A, thus obviating the need for plerixafor.

Methods: All patients undergoing HPC-A collections from April 2009 to May 2010 were reviewed. The predefined protocol was as follows:

All patients started G-CSF 10mcg/kg SQ on day 1.
CD34 cell counts were drawn day 4 of G-CSF.

- If the CD34 cell count ≥ 10, proceed with HPC-A.
- If < 10, an additional evening dose of G-CSF 10mcg/kg was added.

CD34 cell counts repeated day 5.

- If ≥ 10, proceed with HPC-A and continue twice daily G-CSF until the desired CD34 count.
- If the count 1 to 9, G-CSF revert back to once daily and plerixafor was added the evening of day 5 with HPC-A the next morning.
- If < 1, the mobilization attempt was deemed a failure.

Minimum collection goal was 3×10^6/kg CD34.

Results: 86 patients underwent stem collection, of which 69 followed our G-CSF-alone protocol. All 69 were successfully mobilized, 41 (59%) with G-CSF 10mcg/kg SQ daily alone. Of the remaining 28, 18 (64%) mobilized with twice daily G-CSF and 10 (36%) required plerixafor.

Table 1.

	N	Mean CD34/kg	Mean HPC-A Days	Mean Cost per Mobilzation*
Daily G-CSF alone	41	8.15	1.98	$14,757
BID G-CSF	18	6.35	3.17	$23,724
Plerixafor + G-CSF	10	6.45	2.80	$35,863

*HPC-A cost of $6000/day and hospital acquisition cost utilized for G-CSF and plerixafor.Cost savings utilizing our strategy versus plerixafor on day 4 was $219,000 including drug and HPC-A procedure costs. This translates to a cost savings of approximately $8,000 per patient.

Conclusion: Doubling the G-CSF frequency to twice daily on day 4 when the CD34 count was 1- 10 was effective in mobilizing 64% of patients who failed G-CSF-alone mobilization in a similar number of HPC-A days (3.17 vs 2.80) when compared to plerixafor. This strategy results in a significant cost avoidance of approximately $8,000 per patient. Consideration should be given to double-dose G-CSF on day 4 of current ineffective mobilization in lieu of plerixafor.

118

PRELIMINARY EXPERIENCE WITH PLERIXAFOR FOR PERIPHERAL BLOOD STEM CELL MOBILIZATION IN PEDIATRIC PATIENTS

Hawks, R.G.[1], Semidei-Pomales, M.[2], Abendroth, H.E.[1], Garvin, J.H.[1], Cairo, M.S.[1,2,3] [1]Pediatrics; [2]Medicine; [3]Columbia University, New York, NY; [4]New York Presbyterian Hospital, New York, NY

Autologous peripheral blood stem cell (PBSC) transplant is an accepted therapy for pediatric patients with lymphoma, neuroblastoma, and CNS tumors. PBSC mobilization with filgrastim alone or filgrastim following chemotherapy may be unsuccessful in heavily pretreated patients, based on a desired minimum cell count of 2x 10E6 CD34+/kg to proceed with Autologous PBSC transplant. Plerixafor is approved for use in combination with filgrastim for PBSC mobilization, and in adults with lymphoma or myeloma, plerixafor/filgrastim mobilization results in 2- to 3-fold increased likelihood of successful harvest compared to filgrastim alone. We report our experience with plerixafor, utilizing a dose of 240 micrograms/kg SQ 10 -11 hours before pheresis, repeated daily up to 4 days, in 7 pediatric patients (3 refractory Burkitt lymphoma (BL), 1 high risk neuroblastoma (NB), 2 medulloblastoma (MB), 1 recurrent CNS PNET), ages 10 to 20 years, with inadequate or borderline PBSC yields following multiagent chemotherapy and filgrastim. Incremental PBSC yields following filgrastim and plerixafor were 0 to 9.0 × 10E6 CD34+ cells/kg. The Peripheral Blood CD34+ counts varied widely from > 1.0 to 56 cells/uL. 2 of 3 BL patients and the NB patient mobilized successfully and underwent autotransplant. 1 BL patient failed to mobilize and underwent allogeneic transplant. Of 3 CNS tumor patients (all with prior craniospinal irradiation), 1 with MB and 1 with PNET had successful mobilization but died of disease progression prior to autotransplant; the other patient with MB continues on reinduction chemotherapy. No serious adverse events were seen. We conclude that plerixafor is safe and effective in selected pediatric patients even following craniospinal irradiation, but may be less effective in refractory patients with extensive prior chemotherapy. The latter group could potentially benefit from earlier introduction of plerixafor at the first attempted PBSC mobilization.

119

DEFIBROTIDE PREVENTS THE ACTIVATION OF MACROVASCULAR AND MICROVASCULAR ENDOTHELIA CAUSED BY THE SOLUBLE FACTORS RELEASED TO BLOOD BY AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION

Diaz-Ricart, M.[1], Palomo, M.[1], Rovira, M.[2], Escolar, G.[1], Carreras, E.[2] [1]Hospital Clínic, Barcelona, Spain; [2]Hospital Clínic, Barcelona, Spain

Endothelial activation and damage occur in association with autologous hematopoietic stem cell transplantation (HSCT). Several of the early complications associated with HSCT seem to have a microvascular location. Through the present study, we have characterized the activation and damage of endothelial cells of both macro (HUVEC) and microvascular (HMEC) origin, occurring early after autologous HSCT, and the potential protective effect of defibrotide (DF). Sera samples from patients were collected before conditioning (Pre), at the time of transplantation (day 0), and at days 7, 14 and 21 after autologous HSCT. Changes in the expression of endothelial cell receptors at the surface, presence and reactivity of extracellular adhesive proteins, and the signaling pathways involved were analyzed. The expression of ICAM-1 at the cell surface increased progressively in both HUVEC and HMEC. However, a more prothrombotic profile was denoted for HMEC, in particular at the time of transplantation (day 0), reflecting the deleterious effect of the conditioning treatment on the endothelium, especially at a microvascular location. Interestingly, this observation correlated with a higher increase in the expression of both tissue factor and von Willebrand factor on the extracellular matrix, together with activation of intracellular p38 MAPK and Akt. Previous exposure and continuous incubation of cells with DF prevented the signs of activation and damage induced by the autologous sera. These observations corroborate that conditioning treatment in autologous HSCT induces a proinflammatory and a prothrombotic phenotype, specially at a microvascular location, and indicate that DF has protective antiinflammatory and antithrombotic effects in this setting.

120

EFFICACY AND COST-BENEFIT ANALYSIS OF PLERIXAFOR PLUS FILGRASTIM BASED ON A RISK ADAPTIVE APPROACH FOR AUTOLOGOUS PERIPHERAL BLOOD HEMATOPOIETIC PROGENITOR CELL COLLECTION

Vishnu, P.[1], Roy, V.[1], Paulsen, A.[2], Zubair, A.C.[2] [1]Mayo Clinic, Jacksonville, FL; [2]Mayo Clinic, Jacksonville, FL

Plerixafor (P) in combination with filgrastim (F) is currently approved for mobilization of hematopoietic progenitor cells (HPC) in patients with multiple myeloma (MM) or non-hodgkin's lymphoma (NHL). F + P is a very expensive but reduces the incidence of mobilization failure. In an effort to utilize P in a cost efficient manner, we employed a risk adaptive strategy of using P only in patients who are at high risk of mobilization failure defined by peripheral blood $CD34^+$

cell (pCD34) count of < 10/μL after 4 days of F alone. In this study we present the results of efficacy and an estimate of cost of such a risk adaptive strategy for autologous peripheral blood HPC collection. 42 patients with history of NHL or MM undergoing peripheral blood HPC mobilization from February to December 2009 were included in the analysis. All patients received daily filgrastim for 4 days. Our risk adaptive approach was to add P for those 'at-risk' patients, who on day 4 had a pCD34 count of < 10/μL, with apheresis commencing the following morning. Morning administration of F and evening dosing of P was continued daily in this group of 'at-risk' patients for up to a maximum of 4 days or until > 5×10^6 $CD34^+$ cells/kg were collected. Results of consecutive patients who had peripheral blood HPC mobilization were prospectively collected. A decision analytic model was created to estimate the mean cost and effectiveness rates in patients who underwent mobilization with F versus F + P. 18 patients were mobilized with F alone and 24 patients required F + P. Administration of P was safe and no severe adverse events were recorded. Addition of P increased the pCD34 count by 6.8 fold with an average total yield of 4.9×10^6 $CD34^+$ cells/kg. The frequency of poor mobilization among F only and F + P patients was 25% and 7% respectively. The pooled average cost benefit for mobilization with F + P may be up to $ 16,900 per patient and could potentially increase the annual number of transplants by more than 18%. Following autologous stem cell infusion, days to neutrophil and platelet engraftments were similar between the patients who mobilized HPC with F versus F + P (p = 0.12). These results suggest that addition of P to F based on a risk adaptive strategy significantly reduces the frequency of mobilization failures and is also cost effective. Addition of P to F for HPC mobilization has no significant impact on the neutrophil and platelet engraftment.

121

NEUTROPENIC ENTEROCOLITIS (NE) IN ADULT PATIENTS (PTS) UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT): IMPACT OF BOWEL WALL THICKNESS ON CLINICAL OUTCOMES

Jimenez, A.M.[1], Vasoo, S.[2], Maciejewski, J.[1], Rich, E.S.[1], Karmali, R.[1], Venugopal, P.[1], Gregory, S.A.[1], Fung, H.C.[1], Nathan, S.[1] [1]Rush University Medical Center, Chicago, IL; [2]Rush University Medical Center, Chicago, IL

Background: NE is an acute, life-threatening condition characterized by transmural inflammation of the intestinal wall in severely myelosuppressed patients. Although initially described in pediatric leukemia pts it has increasingly been reported in adults with a variety of malignant conditions and in the setting of immunosuppression with HSCT. The aim of this retrospective study was to evaluate the prognostic value of clinical and radiographic findings in HSCT recipients diagnosed with NE.

Patients and Methods: Data from 264 HSCT recipients over a 5 year period was reviewed. 24 pts with a clinical diagnosis of NE supported by the triad of fever, abdominal pain and neutropenia with radiographic evidence of bowel wall thickening (BWT) were identified. Degree of BWT by CT scan [mild (m): 3-6 mm, moderate (M): 6-12 mm and severe (S) > 12 mm] along with clinical characteristics (age, sex, diagnosis, co-morbidities, type of transplant, conditioning regimen and neutropenia length) were evaluated and correlated with clinical outcomes [complicated (CNE) vs. non-complicated (cNE)] and mortality. CNE was defined as those who became bacteremic with enteric flora, required ICU admission or died.

Results: 264 pts underwent a HSCT from 2004 to 2010. A total of 24 (9.1%) pts (average age 52.67 yrs, range 23 – 70yrs) were diagnosed with NE. 14 (58.3%) pts underwent an autologous HSCT and 10 (41.7%) an allogeneic HSCT. Median BWT was 6 mm (range 2 -15 mm). 11 (45.8%) pts had mBWT, 9 (37.5%) pts MBWT and 3 (12.5%) pts SBWT. 13(54.2%) pts had cNE and 11 (45.2%) pts had CNE. 7(29.2%) pts required ICU admission and 3 (12.5%) pts died. Clinical characteristics had no impact on morbidity or mortality in our pt population. Degree of BWT failed to impact mortality on univariate analysis (dead vs. alive: ≥ 3mm p = 0.25, ≥ 6 mm p = 0.48, ≥ 12 mm p = 1.00), but the presence of MBWT and SBWT (≥ 6 mm) was associated with a higher rate of CNE (CNE vs. cNE: ≥ 6 mm p = 0.003 OR:30.0, 95 % CI 2.6-342.7). BWT ≥ 6 mm highly correlated with CNE on multivariate analysis (p = 0.009 OR:31.5 [2.35-422.3]).

Conclusion: Clinical characteristics had no prognostic impact in adult patients who developed neutropenic enterocolitis following HSCT. Patients with moderate and severe bowel thickening have a worse clinical outcome however this failed to predict mortality; likely the result of a small sample size. Larger studies and development of standardized criteria for bowel thickness measurement are warranted.

122

LONG-TERM FOLLOW-UP OF METASTATIC BREAST CANCER PATIENTS RECEIVING HIGHLY PURIFIED AUTOLOGOUS CD34+THY-1+ HEMATOPOIETIC STEM CELLS AFTER HIGH-DOSE CHEMOTHERAPY

Mueller, A.M.S.[1], Kohrt, H.E.K.[2], Laport, G.G.[1], Negrin, R.S.[1], Cha, S.[1], Weissman, I.L.[3], Shizuru, J.A.[1] [1]Stanford University, Stanford, CA; [2]Stanford University, Stanford, CA; [3]Stanford University, Stanford, CA

In the 1990's high-dose chemotherapy (HDCT) with autologous hematopoietic cell transplantation (auto-HCT) was considered a promising, potentially curative treatment approach for patients (pts) with advanced or metastatic breast cancer (MBC). When randomized trials did not confirm a significant benefit of HDCT over standard chemotherapy (CTx) enthusiasm for this therapy fell and transplantation studies ended abruptly. Despite improvements in overall survival (OS) due to better CTx, endocrine, and immunologic agents, MBC remains an incurable disease. One potential reason for the failure of HDCT with auto-HCT is the high rate of occult tumor cell contamination (OTC) in bone marrow, and accordingly in mobilized blood grafts. Here we report the long-term follow-up of 15 pts that underwent HDCT (cisplatin, cyclophosphamide, BCNU) at our institution between 12/96 and 4/98. FACS-purified CD34+Thy1+ hematopoietic stem cells (HSC) with no detectable tumor contamination (detection level 1/106 cells) were used as grafts. Of note, 4/15 leukapheresis products contained OTC prior to sorting. Pts were a median age of 43 years (y), were treated for primary stage IV BC (n = 5), or relapsed BC (n = 10). Status of remission at HCT was CR in 47%, and PR and SD in each 26.5% of pts. More than 12 years after the end of the study 33% pts are alive, 27% in CR. Median progression-free survival (PFS) is 16 months (m), the PFS rate at 3y is 47%, at 10y 27%, each. Median OS for the entire group and for survivors is 120m and 160m, respectively. 5y and 10y OS rates are 60% and 47%, respectively. In comparison, of 78 pts given the same HDCT regimen but unmanipulated grafts, 9% are alive, and 6% without disease, 71% died of their BC, 22% died of other reasons, and 4% were lost to follow-up. Median PFS is 9m, and the PFS rates at 3, 5, and 10y are 18%, 11%, and 8%, respectively. Median OS for the entire group was 26m, and 154m for the 7 survivors. OS rates at 3y, 5y and 10y were 39%, 25%, and 13%, respectively. Even though pts numbers in the HSC group are small, and may include a highly selected population, our data suggest that infusion of a hematopoietic graft, devoid of OTC, may be critical to prolong time to relapse, and increase the proportion of CR. We believe HDCT could regain relevance within multimodal treatment approaches, as a good remission and avoidance of relapse due to OTC in the graft could serve as a foundation for treatment with novel biological and small molecule agents.

123

ADAPTIVE RANDOMIZATION FOR BMT CLINICAL TRIALS WITH BOTH EFFICACY AND FUTILITY OUTCOMES

Sabo, R.T.[1], Roberts, C.H.[2], Toor, A.A.[2], Chung, H.M.[2], Clark, W.B.[2], Edwards, R.W.[2], Anderson, J.[2], Shickle, L.[2], Gorshin, I.[2], McCarty, J.M.[2] [1]Virginia Commonwealth University, Richmond, VA; [2]Virginia Commonwealth University Massey Cancer Center, Richmond, VA

Bone marrow transplant (BMT) clinical trials generally feature fixed randomization schedules determined before patient accruement. Bayesian adaptive designs based on in-trial treatment